

Appl. No. : 09/331,631  
 Fil d : June 21, 1999

### **REMARKS**

The pending claims of the application have been amended to conform the rejoined claims to the amendments made to the Group I claims during prosecution. No new matter has been added by the amendments. Applicants request that Claims 12, 14, 15, 31-33, 36-37, and 39-40 as amended be allowed. Rejoinder of Claims 12, 14-15, 31, 36-37, and 39-40 (Group III in the Restriction requirement) is requested rejoined upon allowance of these claims.

The changes made to the claims by the foregoing amendments are shown herein, including ~~deletions~~ and additions, are shown herein with deletions designated with a strikethrough and additions underlined. No new matter has been added herewith.

### **Summary of the Interview of October 21, 2003**

At the interview of October 21, 2003, the Examiner requested that the Applicants submit a written argument incorporating the statement from the Declaration, *In re Alton* and the Sequence Listing to support Applicants' previous insertion of the language: "x is any amino acid other than cysteine" in the claims and specification. The present Supplemental Amendment is being presented to meet this request.

### **Arguments in support of the language "other than cysteine"**

As explained below, the language "X is any amino acid other than cysteine" is fully supported by the specification.

#### **(a) The Declaration**

The Declaration of Donald James Maclean submitted with Applicants' Preliminary Amendment of April 4, 2002 provides additional evidence concerning the correct interpretation of the specification. In Paragraph 5 of the Declaration, Dr. Maclean concluded that "the phrase 'a cysteine spacing of ...' Would [sic] exclude any other cysteins as an X residue because the protein fragment would no longer conform to the defined cysteine spacing."

#### **(b) *In re Alton***

The proper treatment of a Declaration provided to shed light on the question of whether a patent specification adequately describes the subject matter of a claim was described by the Court

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of Appeals for the Federal Circuit (CAFC) in *In re Alton*, 37 U.S.P.Q.2d 1578 (CAFC 1996). A copy of this decision is provided for the Examiner's reference.

In the *Alton* case, the Applicant's specification explicitly described a modified protein that included two separate modifications. The Applicant included a claim that recited only one of these two modifications. The Examiner rejected this claim as lacking a written description of the specification. In response, Applicant submitted a Declaration from an expert stating that "one of ordinary skill in the art would have understood the specification to describe the two modifications independently and that the description of both modifications together would be relevant as an example of only one of those modifications. . . . Therefore, . . . one of ordinary skill in the art would understand [sic] *Alton* to be in possession . . . of the claimed subject matter." *Alton* at page 1584, column 2. Rather than address this point, the Examiner concluded that the "declaration was inadequate because it did not 'suggest that the written description in the specification supports an interferon-gamma analog which *must* have the claimed structure.'" *Alton* at page 1584, column 1. Thus, the Examiner had concluded that since the specification does not explicitly disclose the embodiment claimed, that the declaration had no merit. The court held that this conclusion was erroneous because it dismissed the "declaration without an adequate explanation of how the declaration failed to overcome the prima facie case initially established." *Alton* at page 1583, column 2.

The declaration submitted in the present case has been treated by the Examiner in the same manner that the court in *Alton* concluded was erroneous. Just as in *Alton*, the present Declaration provided evidence of how one skilled in the art would interpret the specification in response to a written description rejection. The Examiner's response to this Declaration in the latest Office Action (Paper No. 19) mailed April 3, 2003, was to conclude that "the Declaration is not persuasive because the recitation of the negative limitation inserted into the claim by the amendment is new matter as the phrase 'X is any amino acid other than cysteine is not supported by the instant specification.'" Thus, just as in *Alton*, the Examiner dismissed the Declaration because the specification did not explicitly disclose the embodiment claimed. This is precisely the type of conclusion that the CAFC had concluded was erroneous in *Alton*. Accordingly, the Examiner did not provide an adequate explanation of why the declaration failed to rebut the inadequate description rejection, as required by the CAFC.

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(c) The disclosure is implicit to one skilled in the art

One skilled in the art would have known that, although not stated expressly, the language excluding cysteine is an implicit part of the specification and claims. It is abundantly clear from the specification as filed that X could not include cysteine. Claim 1, as originally filed, specifically recited an antimicrobial protein fragment "comprising a *cysteine spacing* of C-3X-C-nX-C-3X-C (SEQ ID NO:38 and 39) wherein n is 11 or 12, X is any amino acid other than cysteine, and C is cysteine" (emphasis added). The emphasized language would have no meaning if X could be cysteine because the inclusion of cysteine would alter the cysteine spacing from the recited spacing.

Further, one skilled in the art would know that the recited cysteine spacing was critical because the cysteine spacing is necessary to provide for the specific S-S bonds necessary to provide an active protein fragment with a specific secondary structure. On page 10 of the specification it is stated:

One aspect of the structure that most likely could not be altered without seriously affecting the structure (and, therefore, the activity of the protein) is the content and spacing of the cysteine residues since this would disrupt the formation of disulfide bonds which are critical to a) maintaining the overall structure of the protein and/or b) making the protein more resistant to denaturation and proteolysis (stabilizing the protein structure). In particular, it is essential that cysteine residues reside on one face of the helix in which they are contained.

Thus, one skilled in the art would know that if X is a cysteine residue, the cysteine spacing would be changed to provide a new position for an S-S bond to form and changing the structure of the peptide. One skilled in the art could readily determine this based on the disclosure of the specification. This is further evidenced by the chapter from the college level biochemistry book by Stryer that was previously provided by Applicants, with their Preliminary Amendment of April 4, 2002. This chapter shows that one skilled in the art would have ample knowledge of the importance of cysteine spacing to conclude that X must not be cysteine.

Finally, as suggested by the Examiner's supervisor at the interview, the specification includes no disclosure of any specific sequence that includes a cysteine residue for X in the formula C-3X-C-nX-C-3X-C. Every sequence listed in the Sequence Listing that fits this formula, or shown in Figure 4, uses an amino acid other than cysteine as X. This further supports the language "X is any amino acid other than cysteine."

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**CONCLUSION**

Should there be any further questions regarding the above-captioned patent application, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Oct. 29, 2003

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